

# **THE USE OF ASPIRIN IN PREGNANCY**

**Daniela Camenzuli**

## **Introduction**

For several years some obstetricians have discouraged pregnant women from taking aspirin as a simple analgesic (De Swiet and Fryers, 1990). This attitude was mainly due to the availability of paracetamol (which is less likely to cause gastric irritation) as well as to studies based on patients taking large doses of aspirin which led to the idea that aspirin taken during pregnancy could lead to teratogenesis (Richards, 1969; Nelson and Forfar, 1971; Saxen, 1975; Zierler, 1985), prolonged gestation (Collins and Turner, 1975; Lewis and Schulman, 1973) and labour (Collins and Turner, 1975; Lewis and Schulman, 1973), maternal and neonatal haemorrhage (Rumack et al 1981; Stuart et al, 1982), premature closure of the ductus arteriosus (Arcilla et al 1969; Levin et al, 1978) and effects on the pulmonary blood vessels (Levin et al, 1978; Perkin et al, 1980).

The possibility that treatment with daily low doses of aspirin (60-75mg) markedly improves perinatal outcome in certain complications of pregnancy postulated to be the result of derangements in prostaglandin biosynthesis, has recently led to the re-examination of the possible adverse effects of aspirin in pregnancy as well as its efficacy. There is a general consensus that low-dose aspirin is both safe and effective in improving perinatal outcome.

This paper mainly aims at assessing the extent of aspirin use by pregnant women in Malta and reasons for use, any adverse effects due to such therapy, its effectiveness and the role of the pharmacist in this field.

## **Methodology**

### **Case Studies**

The birth records from January 1989 to December 1991 were viewed and any cases of mothers with conditions where aspirin may have been used were selected (N=410). Two consultants were contacted. They were shown the list of patients and asked to indicate which of the patients were most likely to be on low-dose aspirin. The mothers' files were then obtained from the Medical Records section of St Luke's Hospital and the patients' treatment together with outcome were studied.

## **Urine Tests**

During their antenatal visits, patients sometimes hide the fact that they are using aspirin (Collins and Turner, 1975). 158 patients attending the antenatal clinic at St Luke's Hospital were therefore questioned regarding medication they used during their pregnancy and asked specifically whether they used aspirin. Their urine samples were then tested with 10% ferric chloride solution to detect surreptitious use. Urine samples in amber-coloured bottled or in containers which made it difficult to note if there was a colour change were excluded from the study (N=32).

## **Survey 1**

100 patients attending the antenatal clinic at St Luke's Hospital were interviewed, mainly to assess whether they used aspirin, their confidence in the pharmacist's advisory role and to study the medication most frequently used in pregnancy (especially if these interact with aspirin therapy).

## **Survey 2**

25 questionnaires were personally given to consultants, registrars and senior house officers at the Obstetrics and Gynaecology Department of St Luke's Hospital.

## **Survey 3**

Questionnaires were personally given to 51 Maltese pharmacists and information was drawn from the pooled results.

## **Results**

### **Case Studies**

Only 6 files were found to specify that the patient was on low-dose aspirin therapy. The information gathered is shown in Table 1.

**Table 1:** Details of patients studied, complication treated with aspirin and outcome of therapy

Case number	1	2	3	4	5	6
Patient's age	29	37	31	35	27	24
Parity	1	0 <sup>3</sup>	1	1	0	1
Complication	SLE	RA	PIH/ PE	PIH/ IUGR	PIH	PIH IUGR
Dose (mg)		75	75	75	75	75
Outcome	alive	alive	alive	alive	alive	alive
Gestation	38 <sup>-2</sup>	35 <sup>+5</sup>	33	28	39	38
Birthweight/kg	3.170	2.800	1.900	1.050	3.340	3.300
APGAR score	6:9	9:10	9:10	9:9	6:9	4:6:9
Caesarian	-	+	+	+	-	+
Blood loss	normal	normal	normal	normal	<200ml	normal
Malformations	none	oes.at.	none	none	none	none

Key:	SLE:	systemic lupus erythematosus
	RA:	recurrent abortion
	PIH:	pregnancy-induced hypertension
	PE:	pre-eclampsia
	IUGR:	intra-uterine growth retardation
	Oes.at.:	oesophageal atresia

### Urine Tests

The results obtained in the iron (III) chloride on the patients' urine samples are shown in Table2, whilst Figure 1 shows the medications that were used in pregnancy by the 126 mothers interviewed.

Table 2: Results of Urine Test

N=126	Urine Test		Used Apirin	
	Negative	Positive	Yes	No
Number of mothers	126	0	1	125
Percentage	100	0	0.79	99.21

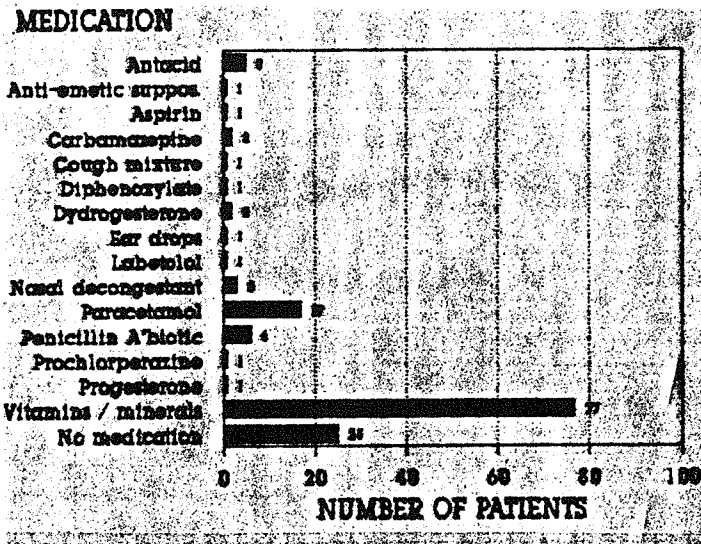


Figure 1: Medications used in Pregnancy by 126 mothers attending the Antenatal Clinic at St Luke's Hospital

## Survey 1

Of the 100 patients interviewed, 4% were using 75mg aspirin daily, as prescribed by their doctor. One of these patients experienced heart burn but did not attribute this to her aspirin therapy.

The other 96% of patients claimed to have never used aspirin in any of their pregnancies, either because there never use aspirin usually (n=51), or because aspirin and medicines in general are contra-indicated in pregnancy (n=19 and n=34 respectively), or because they do not know how to swallow and so never take medicines (n=2). 4 of these patients said that they try to do without any medication whatsoever when they are pregnant.

It is interesting to note, however, that one patient actually took aspirin at some point during her pregnancy without knowing it (Disprin<sup>R</sup>).

Only 26% of the patients ever asked the pharmacist for advice regarding the use of medications in pregnancy, mostly to allay worries regarding any medications they may have had to take.

94% of the patients were taking medications during their pregnancy. These included most of the medications indicated in Figure 1 (except for progesterone, diphenoxylate and prochlorperazine maleate), as well as oral rehydration salts, sore throat lozenges, diazepam, clotrimazole cream, miconazole and insulin.

## Survey 2

Of the 19 doctors who answered the questionnaire, 94.7% (n=18) were of the opinion that aspirin could be useful in pregnancy. 89.5% (n=17) of these doctors have in fact prescribed aspirin for certain pregnant patients who, in their professional opinion, may have benefited from such therapy.

**Table 3: Conditions for which 75mg Aspirin has been prescribed by doctors at the Antenatal Clinic at St Luke's Hospital**

Condition	% Doctors
Severe pregnancy-induced hypertension	63.2
Intra-uterine growth retardation	68.4
Lupus anticoagulant (SLE)	47.4
Recurrent abortion	42.1
Simple analgesia	5.3
Varicose veins	5.3
Prophylaxis of pre-eclampsia	5.3
Superficial phlebitis	5.3
Premature labour contractions	5.3
Common cold	5.3
Deep vein thrombosis	5.3
Renal transplant in pregnancy	5.3

Few doctors claimed that aspirin caused side effects in any of their patients. Gastro-intestinal irritation was the main adverse effect reported (41.2%, n=7) even with low-dose aspirin. There was one reported incident (5.3%) of a patient on 75mg aspirin daily who presented with haematemesis soon after starting therapy - she had no previous relevant history. Another side-effect reported by one doctor (5.3%) was thrombocytopenia in a neonate.

84.2% (n=16) of the doctors think that the pharmacist has an important role in preventing adverse effects due to aspirin ingestion during pregnancy.

### Survey 3

Of the 42 pharmacists who answered the questionnaire, only 21.4% were aware of the new uses of aspirin in pregnancy. All the pharmacists felt that they should know more about the use of aspirin in pregnancy and would appreciate the publication of a leaflet or some other source of information regarding its use and potential adverse effects.

## Discussion

Aspirin has been prescribed by obstetricians in Malta. Although, apart from the neonate with oesophageal atresia in Case 1, there was no evidence of adverse effects in any of the case studies, these did occur following low-dose aspirin therapy (as indicated by the survey for obstetricians).

The 100% negative result in the ferric chloride test for salicylates in urine indicates that Maltese mothers are conscious of the dangers of drug-taking during pregnancy (this was further confirmed in the patient interviews). Thus, although this simple and cheap test may alert the obstetrician to a factor that may not be disclosed by patients during their antenatal visits<sup>6</sup>, there is no basis for strongly recommending its introduction at the antenatal clinic of St Luke's Hospital.

Aspirin was found to interact with 3 of the medications being used by the patients interviewed, these were antacids, metaclopramide and labetolol.

## Conclusions

Maltese mothers are very keen to learn more about anything to do with their pregnancy. This was clearly evident whilst carrying out the patient interviews in the antenatal clinic waiting room, since the patients asked various questions which they could have easily asked a community pharmacist. This indicates that the set-up of the antenatal clinic is ideal for patient education and the availability of a pharmacist would be of great benefit for the patients. It would also be useful to have other forms of patient education, such as videos, etc. in the waiting rooms to occupy the patients' time usefully, whilst satisfying their great urge to learn more.

The pharmacist has an important contribution to give in reducing the incidence of adverse effects of low-dose aspirin therapy. Many patients (as indicated by the patient using Disprin<sup>R</sup>) do not know that certain preparations contain aspirin and it is important for the pharmacist to make the patient aware of this when dispensing the preparation. Other ways in which the pharmacist may prevent adverse effects is by:



- knowing the pharmacological effects of aspirin and hence its side effects and the possibility of aspirin allergy
- avoiding dispensing high dose aspirin to pregnant patients
- checking the dose prescribed and advising the patient to only take the recommended dose
- consulting a doctor in cases where he/she thinks that aspirin treatment is indicated
- advising the patient to take the preparation after meals and dispensing better-tolerated formulations
- advising on use/misuse, side effects and possible drug interactions
- advising the patient on the benefits of low dose aspirin when this is prescribed and reassuring her that such therapy would have no side-effects on the baby if administered as recommended

The community pharmacist is in an ideal position to monitor any medications (whether prescribed or not) being taken by the patient, to check for any drug interactions or whether these are contra-indicated in pregnancy.

To be able to offer the service outlined above, the pharmacist must keep abreast with the latest findings and be well-informed about the new uses of low-dose aspirin in pregnancy. A booklet was therefore compiled, so as to be sent to all pharmacists in Malta and Gozo (including those who did not participate in the survey).

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